

Please replace the paragraph starting at page 60 line 7 with the following rewritten paragraph:

--An alternative β -secretase assay utilizes internally quenched fluorescent substrates to monitor enzyme activity using fluorescence spectroscopy in a single sample or multiwell format. Each reaction contained 50 mM Na-MES (pH 5.5), peptide substrate MCA-EVKMDAEF[K-DNP] (SEQ ID NO: 58) (BioSource International) (50 μ M) and purified Hu-Asp-2 enzyme. These components were equilibrated to 37 °C for various times and the reaction initiated by addition of substrate. Excitation was performed at 330 nm and the reaction kinetics were monitored by measuring the fluorescence emission at 390 nm. To detect compounds that modulate Hu-Asp-2 activity, the test compounds were added during the preincubation phase of the reaction and the kinetics of the reaction monitored as described above. Activators are scored as compounds that increase the rate of appearance of fluorescence while inhibitors decrease the rate of appearance of fluorescence.--

IN THE SEQUENCE LISTING

Please replace the existing sequence listing as filed (54 pages) with the substitute sequence listing filed herewith (43 pages).

IN THE CLAIMS

Please cancel all pending claims.

Please add following new claims 151-300.

--151. A purified polypeptide comprising a mammalian Asp2 polypeptide that cleaves a mammalian β -amyloid precursor protein (APP), or a fragment, analog, or derivative of said mammalian Asp2 polypeptide that retains the APP cleaving activity.

152. A purified polypeptide according to claim 151, selected from the group consisting of:

(a) a polypeptide comprising a purified human Asp2(a) amino acid sequence set forth in SEQ ID NO: 4 or a fragment thereof that cleaves APP;

(b) a polypeptide comprising a purified human Asp2(b) amino acid sequence set forth in SEQ ID NO: 6 or a fragment thereof that cleaves APP;

(c) a polypeptide comprising the murine Asp2 amino acid sequence set forth in SEQ ID NO: 8, or a fragment thereof that cleaves APP;

(d) a polypeptide comprising a purified polypeptide having an amino acid sequence that is at least 95% identical to (a), (b), or (c).

153. A purified polypeptide according to claim 151, comprising a purified human Asp2(a) amino acid sequence set forth in SEQ ID NO: 4 or a fragment thereof that cleaves APP.

154. A purified polypeptide according to claim 151, said polypeptide comprising a portion of the human Asp2(a) amino acid sequence set forth in SEQ ID NO: 4, said portion including amino acids 22-501 of SEQ ID NO: 4 and lacking amino acids 1-21.

155. A polypeptide according to claim 154, beginning with the N-terminal sequence ETDEEP.

156. A purified polypeptide according to claim 151, said polypeptide comprising a portion of the human Asp2(a) amino acid sequence set forth in SEQ ID NO: 4 effective to cleave APP, said polypeptide lacking transmembrane domain amino acid residues 455-477 of SEQ ID NO: 4.

157. A polypeptide according to claim 155, said polypeptide lacking amino acids 454-501 of SEQ ID NO: 4.

158. A purified polypeptide according to claim 151, comprising a purified human Asp2(b) amino acid sequence set forth in SEQ ID NO: 6 or a fragment thereof that cleaves APP.

159. A purified polypeptide according to claim 151, said polypeptide comprising a portion of the human Asp2(b) amino acid sequence set forth in SEQ ID NO: 6, said portion including amino acids 22-476 of SEQ ID NO: 6 and lacking amino acids 1-21.

160. A purified polypeptide according to claim 151, said polypeptide comprising a portion of the human Asp2(b) amino acid sequence set forth in SEQ ID NO: 6 effective to cleave APP, said polypeptide lacking transmembrane domain amino acid residues 430-452 of SEQ ID NO: 6.

161. A purified polypeptide according to claim 151, comprising the murine Asp2 amino acid sequence set forth in SEQ ID NO: 8, or a fragment thereof that cleaves APP.

162. A purified polypeptide according to claim 151 comprising a fragment of a mammalian Asp2 polypeptide, wherein the purified polypeptide lacks the transmembrane domain of said mammalian Asp2 polypeptide.

163. A fusion protein comprising a polypeptide of claim 151, and which further includes a heterologous tag amino acid sequence.

164. A polypeptide of claim 151, wherein the polypeptide cleaves human APP or human APP-Sw at the β -secretase recognition site.

165. A polypeptide of claim 151, wherein the polypeptide lacks any mammalian Asp2 pro-peptide sequence.

166. A polypeptide according to claim 151, selected from the group consisting of:
(a) a polypeptide comprising a portion of the amino acid sequence set forth in SEQ ID NO: 4 effective to cleave APP, wherein the polypeptide lacks amino acids 1-45 of SEQ ID NO: 4; and